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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/887,853

06/21/2001

L. L. Houston

PP00926.106

9213

2300-0926.05

7590

02/14/2006

EXAMINER

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ART UNIT

PAPER NUMBER

1643

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/887,853

Applicant(s)

HOUSTON ET AL.

Examiner

Karen A. Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 77-86 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 77-85 is/are rejected.
- 7) ☐ Claim(s) 86 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

Claims 77-86 have been amended and are under consideration.

Sections of Title 35, U.S. Code not found in this action can be found in a prior action.

It is noted that the phrase "consistign essentially of" is interpreted as "comprising" absent a specific limiting definiton in the specification. M.P.E.P. 2111.03

For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355

The rejection of claims 77-85 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 22-24 of U.S. Patent No. 5,534,254 in view of Huston et al (WO 88/09344) is maintained for reasons of record.

Claim 77 is drawn to a monomeric single-chain Fv(sFv)molecule comprising (a) a first polypeptide domain comprising CDR interposed between framework regions derived from human immunoglobulins and having the general formula FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, and (b) a second polypeptide domain comprising CDRs interposed between framework regions derived from human immunoglobulins and having the general formula FR1'-CDR1'-FR2'-CDR2'-FR3'-CDR3'-FR4', wherein CDR1, CDR2, CDR3, CDR1', CDR2' and CDR3' are residues 31-35, 50-66, 99-104, 157-167, 183-189 and 222-240, respectively, of SEQ ID NO:6, and wherein said first and said second domains together are capable of forming a binding site for c-erbB2. Claim 78 embodies the sFv of claim 77 wherein said first and second polypeptides are capable of forming a humanized antibody. Claim 79 embodies the sFv of claim 78 wherein the FR sequences are from a human myeloma antibody. Claims 80 and 83 embody the sFv of claim 77 wherein the first and second peptide domains are linked by a polypeptide linker. Claims 81 and 84 embody the sFv of claim 80 and 83 wherein the polypeptide linker comprises at least 10

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amino acids. Claims 82 and 84 embody the sFv of claim 81 and 84 wherein the polypeptide linker comprises SEQ ID NO:7 [(Gly4Ser)3].

Claims 1 and 2 of the '254 patent are drawn to a composition comprising *an sFv* comprising two separate polypeptide chains, each of which have an amino acid sequence comprising two polypeptide domains connected by a polypeptide linker sequence, the amino acid sequence of said domains comprising CDR regions interposed between framework regions, the framework regions and CDRs of each sFv defining a binding site for an antigen, Claim 22 embodies the compositions of claims 1 or 2 wherein the framework sequences are derived from a human antibody. Claim 23 embodies the compositions of claims 1 or 2 wherein said CDR sequences are derived from an immunoglobulin that binds to the c-erbB-2 antigen. Claim 24 embodies the composition of claim 23 wherein CDR sequences are derived from 520C9. The claims of the patent do not specify the amino acid sequences of the CDR regions derived from the 520C9 antibody, or the polypeptide linker sequence of SEQ ID NO:7.

Huston et al teach a method of making humanized antibodies (Legend for Figure 5 and page 23, lines 4-16) and *single chain antibodies* comprising the generalized formula FR1-X1-FR2-X2-FR3-X3-FR4- (page 43, lines 20-28), and the linker sequence, (Gly4Ser)3, for connecting two polypeptide domains which does not interfere with domain folding and has little propensity for secondary structure, but is short enough so that both polypeptides can interact (page 52, lines 10-23). Huston et al teach a construct comprising a master human immunoglobulin framework which may be used to insert any human CDR sequence (page 51, lines 4-8).

The instant claims are obvious over the claims of the '254 because claim 22 of the patent specifies human framework regions, and claims 23 and 24 require CDR regions derived from the 520C9 antibody, wherein said antibody binds to c-erbB-2. It would be obvious to one of skill in the art to sequence the polynucleotides encoding the 520C9 antibody and use the sequence information in the same way as Huston et al to express a sFv comprising the CDR of the heavy chain of 520C9 interspersed between human immunoglobulin framework regions, and a sFv comprising the CDR of the light chain of 520C9 interspersed between human immunoglobulin framework regions and join both sFv by the linker sequence (Gly4Ser)3. One of skill in the art

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would have been motivated to do so by the teachings of Huston et al on how to express sFv having human framework regions, and how to link two sFv comprising a heavy chain region to a sFv comprising a light chain region by means of the linker sequence (Gly4Ser)₃ which held the two sFv at an appropriate distance for interaction to form an antigen-binding site, but which did not interfere in the secondary structure of the sFv.

Applicants amendment to sFv was insufficient to overcome the outstanding double-patenting rejection.

Claim 86 remains objected to for being dependent on a rejected claim.

All other rejections and objections as set forth in a previous Office action are withdrawn.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

2/6/2006


KAREN A. CANELLA PH.D.
PRIMARY EXAMINER